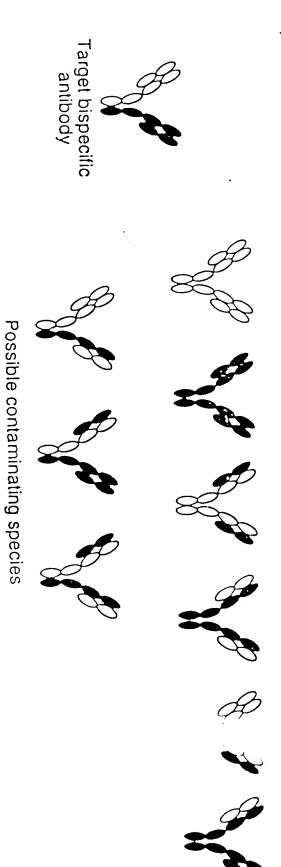
A) Before engineering of CH3 domain



B) After engineering of CH3 domain

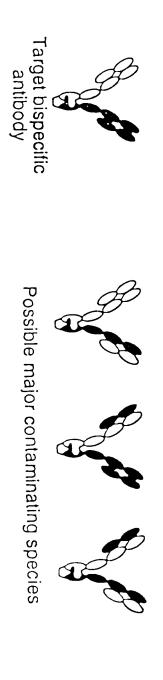
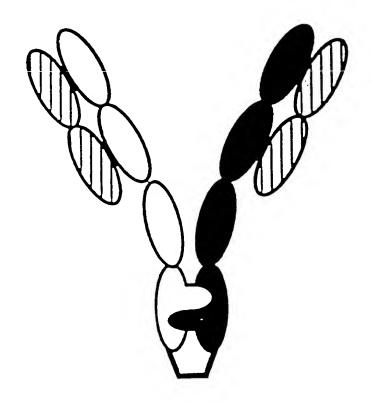


Fig. 1B

¬ = Engineered disulfide bond between CH3 domains



Target bispecific antibody

Fig. 2A

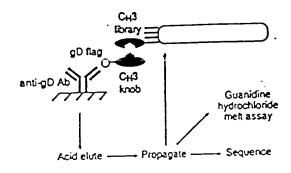


Fig. 2B

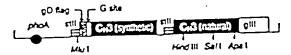
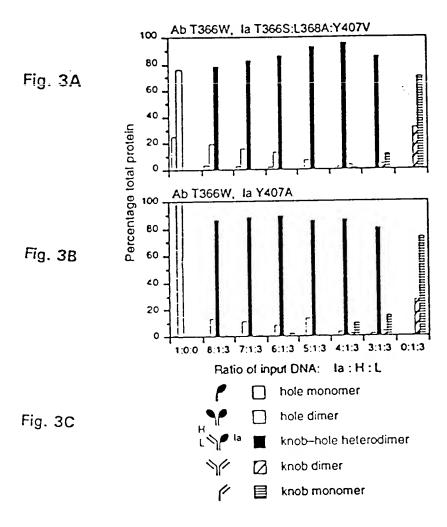


Fig. 2C

(SEQ ID NO: 13)



	~
AX1.78	OSV
Rse.23	VSQ.
IGER. MAT2C1	\S\
GCSFR.A4	QS/
Rse.04	QS/
obr.4	VSQ.
Rse.20	QS/
Rse.15	QS/
vegf.5	05

/LTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV /LTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV 1LTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV J.TQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGK<u>G</u>PKLMIYEGSKRPSGV JTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV LTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGK<u>G</u>PKLMIYEGSKRPSGV VLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV VLTQPASVSGSPGQSITISC<u>TGTSSDVGGXNYVS</u>WYQQHPGKAPKLMIY<u>EGSKRPS</u>GV /LTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV ######### abc 30

CDR L2

14)	15)		7 6) C			
C	. ON		IDN QI				TON CIT	
۲ د	D I	ID	D I	ID				1
(91 . ON OT CES,	SEO ID NO:	(SEQ ID NO:	(SEQ	(SEQ	(SEQ	(SEQ	(SEC)	
	SNRFSGSKSGNTASLTISGLQAEDEADIICSSIIITKSIIVI GGSIXATTA	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SNRFSGSKSGSTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SNRFSGSKXGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SNRFSGSKSGNTASLTISGLQAEDEADYYC <u>SSYTTRSTRV</u> FGGGTKLTVL

IGER.MAT2CI GCSFR.A4

Rse.23

AX1.78

Rse.20

Rse.04

obr,4

vegf.5

Rse.15

CDR L3 V_{H} her3.18 10 20 <u>30</u> ab 40 QVQLVQSGGGLVQPGGSLRLSCAASGFTFSSYEMN--WVRQAPGKGLEWVSGISGSGGSTYY EVQLVESGPGLVKPSQTLSLTCTVSGGSI\$SGGYYWSWIRQHPGKGLEWIGYIY-YSGSTYY CDR H1 obr.26 110 100abcde 90 80 abc 70 60 (SEQ ID NO: 23) <u>ADSVKG</u>RFTISRDNSKNTLYLQMNRLRAEDTAVYYCAR<u>DNGWELTDWYFDL</u>WGRGTMVTVSS * ** ** **** NPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARVDLEDYGSGASDYWGQGTLVTVSS (SEQ ID NO: 24) CDR H3 CDR H2 V_L 50___ 40 20 ____30___ her3.18 10 DIQMTQSPSTLSASIGDRVTITCRASEGIYHWLAWYQQKPGKAPKLLIYKASSLASGAPSRF CDR L2 CDR L1 obr.26 90_____100 80 70 SGSGSGTDFTLTISSLQPDDFATYYCOOYSNYPLTFGGGTKLEIK (SEQ ID NO: 25) CDR L3

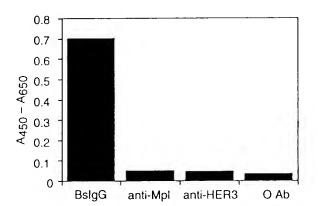
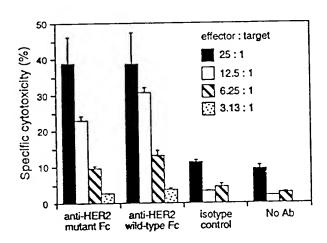


Fig. 6



Percentage Identity of anti-ObR and anti-HER3 $V_{\scriptscriptstyle L}$

	Н1	Н2	Н3	Н4	Н5	н6	н7	н8_	Н9	н10	H11
01	49	47	51	81	60	48	76	51	100	62	51
02	84	79	88	50	48	99	48	88	48	45	88
03	83	82	85	51	50	95	49	85	49	46	85
03	47	50	51	83	77	48	65	51	73	64	51
05	49	47	51	81	60	48	76	51	100	62	51
06	83	79	86	50	50	99	47	86	48	45	86
07	81	100	86	51	49	80	48	86	47	44	86
08	81	100	86	51	49	80	48	86	47	44	86
1	81	100	86	51	49	80	48	86	47	44	86
09		79	85	50	49	98	46	85	48	45	85
010	83	80	87	50	49	99	47	87	48	45	87
011	83		86	51	49	80	48	86	47	44	86
012	81	100.	51	81	60	48	76	51	100	62	51
013	49	47		95	67	49	76	54	75	62	54
014	50	50	54	49	48	97	46	85	47	44	85
015	82	79	85			100	47	87	48	45	87
016	84	80	87	50	49		3	47	62	100	
017	45	44	47	65	62	45	62			62	50
018	50	51	50	75	79	50	63	50	66	02	0.0

O1-018: Anti-Ob-R antibody clones obr. 1, 11, 12, 14, 15, 16, 17, 18, 19, 2, 20, 21, 22, 23, 24, 26, 3, 4, respectively.

H1-H11: Anti-HER3 antibody clones her3.1, 3.10, 3.11, 3.12, 3.16, 3.18, 3.19, 3.22, 3.3, 3.4, 3.7, respectively.